REMARKS

The Office Communication mailed February 13, 2003 stated that the instant application would be treated as an RCE, and that the restriction requirement originally mailed June 6, 2002 was outstanding.

Status of Claims

Claims 1-48 are pending in this application, new claims 45-48 having been added, and claims 30-44 withdrawn from consideration. Support for new claims 45-48 can be found throughout the specification and in original claims 1, 5, and 27, and thus contain no new matter. The newly added claims correspond to Restriction Group I in that they are directed to methods of treating connective disorders by transplantation of recombinant cells.

Response To Restriction Requirements

Applicant elects Group I, claims 1-29, and newly added claims 45-48, with traverse. According to the MPEP, where claims can be examined together without undue burden, the Examiner must examine the claims on the merits even though they are directed to independent and distinct inventions. See, the MPEP at 803.01. In establishing that an "undue burden" would exist for co-examination of claims, the Examiner must show that examination of the claims would involve substantially different prior art searches, making the co-examination burdensome. To show undue burden resulting from searching difficulties, the Examiner must show that the restricted groups have a separate classification, acquired a separate status in the art, or that searching would require different fields of search (MPEP at § 808.02). Applicants respectfully submit that all of the inventions in the present application can readily be searched without undue burden.

In response to the Examiner's further requirement of a single species in claims 1, 2, 4, 5, 10, 14, 17, 22 and 27 of Restriction Group I, Applicants respectfully submit that there are no grounds for this additional restriction. Applicants have presented generic claims directed to methods of treating a connective tissue disorder. According to MPEP 809.02(c)(B)(1), when a generic claim is subsequently found to be allowable, all non- elected species embraced by non-

elected claims are no longer withdrawn since they are fully embraced by the allowed generic claim.

Nonetheless, in order to be fully responsive to the Restriction Requirement, the claims of Group I have been amended to comply with the Examiner's further requirement. Claim 1 has been amended and new claim 45 has been added to elect the soluble IL-1 receptor recited in original Claim1. Claim 2 and Claim 3 have been amended to elect connective tissue cells and synovial cells respectively as the target cells to be transduced by the methods of the invention. Claim 4 has been amended to elect the joint space as the site of delivery of the transduced cells. Claim 5 has been amended, and new claim 46 has been added, to elect IL-10 as recited in original Claim 5. Claim 10 has been amended to elect IGF. Claim 14 has been amended to elect the TIMPS. Claim 17 has been amended to elect adenovirus as the recombinant vector. Claim 22 has been elected to elect sIL-1R as the therapeutic protein of interest. Claim 27 has been amended, and new claim 48 has been added to elect IRAP as the gene of interest recited in original claim 27.

As per Examiner Shukla's request, a clean copy of all pending claims is attached.

In light of the above, Applicants respectfully request that the restriction be withdrawn. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 326-2422.

Respectfully submitted,

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Pending Claims

1. (Currently amended) A method for treating a connective tissue disorder in a mammalian host, the method comprising transducing a population of target cells with a recombinant vector encoding a therapeutic protein, or a biologically active derivative or fragment thereof, and transplanting said transduced cells into the mammalian host, such that subsequent expression of the therapeutic protein, or a biologically active derivative or fragment thereof within the host reduces at least one deleterious joint pathology or indicia of inflammation normally associated with a connective tissue disorder.

2. (Currently amended) The method of Claim 1, wherein said target cells are connective tissue cells.

3. (Currently amended) The method of Claim 2, wherein said connective tissue cells are synovial cells.

4. (Currently amended) The method of Claim 3, wherein said transduced cells are transplanted at a joint space of said host.

5. (Currently amended) The method of Claim 2, wherein said therapeutic protein is a cytokine.

6. (Currently amended) The method of Claim 5, wherein said cytokine is BMP, selected from the group consisting of BMP-1, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8 and BMP-9.

7. (Original) (Original) The method of Claim 6, wherein said BMP is selected from the group consisting of BMP-2 and BMP-7.

8. (Currently amended) The method of Claim 5, wherein said cytokine is vIL-10.

9. (Currently amended) The method of Claim 5, wherein said cytokine is growth hormone.

10. (Currently amended) The method of Claim 5, wherein said cytokine is IGF.

11. (Currently amended) The method of Claim 10, wherein said IGF is selected from the group consisting of IGF-1 and IGF-2.

12. (Currently amended) The method of Claim 2, wherein said therapeutic protein is a soluble IL-1 receptor selected from the group consisting of soluble IL-1 receptor Type 1 and soluble IL-1 receptor Type II.

13. (Currently amended) The method of Claim 2, wherein said therapeutic protein is a soluble TNF-α receptor selected from the group consisting of soluble TNF-α receptor Type I and soluble TNF-α receptor Type II.

14. (Currently amended) The method of Claim 2, wherein said therapeutic protein is a proteinase inhibitor selected from the group consisting of TIMP-1, TIMP-2, TIMP-3, TIMP-4.

15. (Original) The method of Claim 2, wherein said recombinant vector is selected from the group consisting of a viral vector and a non-viral vector.

16. (Withdrawn).

17. (Currently amended) The method of Claim 15, wherein said recombinant vector is an adenovirus.

18. (Withdrawn).

19. (Original) The method of Claim 15, wherein said recombinant vector is a Plasmid DNA vector.

20. (Currently amended) The method of Claim 2, wherein transplantation of transduced cells is by intraarticular injection.

21. (Currently amended) The method of Claim 3, wherein said synovial cells are autologous synovial cells.

22. (Currently amended) The method of Claim 15, wherein the viral vector is an MFG vector and the therapeutic protein, or a biologically active derivative or fragment thereof is sIL-lR.

23. (Currently amended) The method of Claim 22, wherein the therapeutic protein, or a biologically active derivative or fragment thereof is selected from the group consisting of sIL-1R Type I, and sIL-lR Type II.

24. (Withdrawn).

25. (Currently amended) The method of Claim 22, further including the step of storing said population of transduced cells prior to transplantation.

26. (Currently amended) The method of Claim 25, wherein said population of transduced connective cells are stored in 10% DMSO under liquid nitrogen prior to transplantation.

27. (Currently amended) A method for treating a connective tissue disorder, comprising:

introducing one or more DNA sequences encoding one or more genes of interest into at least one target cell of a host by employing non-viral means selected from the group consisting of liposome, calcium phosphate, electroporation, DEAE-dextran and injection of

naked DNA such that subsequent expression of said gene or genes within said host reduces at least one deleterious joint pathology or indicia of inflammation normally associated with a connective tissue disorder.

28. (Original) The method of Claim 27, including employing a liposome selected from the group consisting of CD-cholesterol and SF-cholesterol.

29-44. (Withdrawn).

45. (New) The method of Claim 1, wherein the therapeutic protein or biologically active derivative or fragment thereof is soluble IL-1 receptor.

46. (New) The method of Claim 5, wherein the cytokine is IL-10.

47. (New) The method of Claim 5, wherein the cytokine is BMP.

48. (New) The method of Claim 27, wherein the gene of interest is IRAP.